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(71) Applicant *(for all designated States except US)*: **QUICK-COOL AB** [SE/SE]; Ole Römers väg 12, S-223 70 Lund (SE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LUNDERQVIST, Anders** [SE/SE]; Svenska vägen 48, S-226 39 Lund (SE). **ALLERS, Mats** [SE/SE]; Kävlingevägen 106, S-226 50 Lund (SE). **BORIS-MÖLLER, Fredrik** [SE/SE]; Stora Tomegatan 14, S-223 51 Lund (SE). **WIELOCK, Tadeusz** [SE/SE]; Stora Gråbrödersgatan 3 A, S-222 22 Lund (SE).

(74) Agent: **STRÖM & GULLIKSSON AB**; P.O. Box 4188, S-203 13 Malmö (SE).

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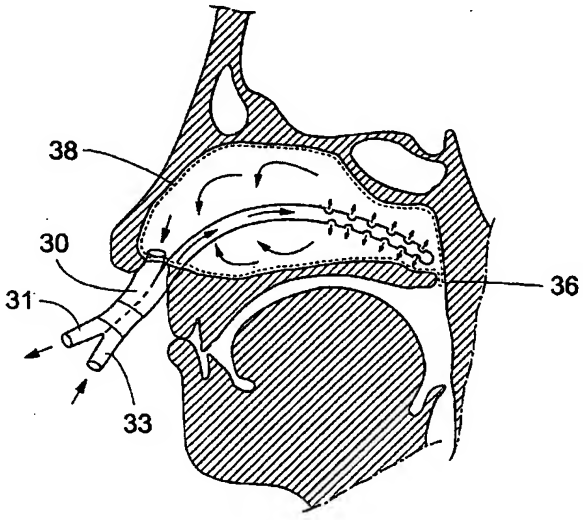
(54) Title: CEREBRAL TEMPERATURE CONTROL



(57) Abstract: A system (10) for cerebral temperature control of a human being; comprising a double lumen catheter (30) to be introduced through a nostril of a human being and to be placed with its tip at the level of the back of the tongue. The double lumen catheter means (30) comprises a first lumen (32) and a second lumen (38) being in fluid communication by means of a set of end openings (34). The second lumen is configured as an expandable balloon. A temperature regulator is connected to the reservoir (20) comprising the cooling fluid for regulating the temperature of the fluid. A pump circulates the fluid. Alternatively, the fluid is fed by gravity.

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TITLE: CEREBRAL TEMPERATURE CONTROL

Technical field of the invention

The present invention refers to the control of the temperature of the brain of a human being, and especially to cooling of the brain.

Background of the invention

In pathological conditions, the body temperature or the temperature of body parts of a human being influences the healing process and the risk of permanent damage. Cancer cells, for example, are heat sensitive and a local heating of the blood flow around a cancer tumor may for some types of cancer constitute a treatment resulting in restrained tumor growth or in some cases even in a shrinking of the tumor. In other cases cooling of a body part may be important to reduce adverse secondary symptoms of the pathological condition, this is primarily intended for the treatment of brain ischemia.

In the case of a stroke, the blood flow to the brain is reduced (ischemia) due to a hemorrhage or the clogging of a blood vessel. This condition will cause permanent functional deficits unless treatment to restore blood flow and protect nerve cells is initiated at an early stage, which will reduce the loss of bodily functions, such as paralysis. It is well known that cooling the brain effectively blocks the development of cellular damage after an episode of ischemia.

Whole body cooling of the patient suffering transient circulatory arrest to the brain results in a reduction of the symptoms of neurological deficit. However, there are certain problems associated with whole body cooling. One is that the cooling is not fast enough to effectively use its protective potential. Another problem is that whole body cooling must be carried out under close control of physiological parameters or under anesthesia. Yet another problem is that there is a risk of cardiovascular complications.

In the case of a circulatory arrest, the brain can suffer permanent damage if the arrest exceeds a time period of about 5-15 minutes. However, if the temperature of the brain is lowered before, during or after the arrest, the brain damage is diminished.

In the case of brain trauma the brain suffers from open or close head concussion. Hypothermia has been shown to diminish traumatic brain injury in such cases.

There are several methods in the prior art to carry out a more isolated cooling of a single organ or body part. An example of cooling of the brain in a human being is disclosed in the patent document WO 98/23217, relating to a method of cerebral retro-perfusion and retro-infusion, involving the cooling of arterial blood that then is returned to the entire brain. However, this method entails a large and complicated surgical procedure, which delays the onset of an actual treatment.

US 5,906,588 discloses a method and a device for heart-lung bypass and cooling of a specific body part. This disclosure primarily relates to complicated heart surgery and organ transplantation.

The US patent application 10/072,857 discloses a first phase comprising the step of introducing an infusion catheter for infusion of a temperature controlled infusion solution or perfusate into a vein initiating quick general body hypothermia. An optional second phase may be used, wherein a second infusion catheter is introduced into an artery of the human being, the second infusion catheter being configured to provide selective temperature control of the brain and infusion of other important substrates and pharmacological compounds into the brain. A third phase is also disclosed, wherein an extra-corporeal circuit is established between a vein and an artery. Blood is withdrawn from the vein, and the temperature of the blood is modified outside the body and the blood is returned to the body through the artery.

In many animals, the brain can be protected from overheating by heat exchange over the rete mirabile at the base of the brain. Here a fine network of the carotid artery is in close connection to a similar network of veins draining the brain. Respiratory evaporation from the surfaces of the nostrils and the epipharynx cools veins in this region flowing towards the rete mirabile whereby heat exchange can occur between arteries and veins. In animals without a rete mirabile, a variation of more or less complicated scrolls of conchae in the nasal cavity enhances evaporation and the heat exchange.

Flushing the nasal cavities with fluids have been shown to reduce the brain temperature (Natale J E et al Stroke 1989; 20:770-777, Hagioka S et al. Crit. Care. Med. 2003; 31:2502-2508). To prevent the flushing fluid to enter the trachea, however, tracheostomy or intubations are nec-

essary and still it would be difficult to prevent fluid to enter the esophagus.

Disclosure of the invention

The present invention is based on the discovery that the cerebral arteries can temper the human brain by remnants of the venous carotid rete, i.e. the cavernous and other sinuses, surrounding the carotid and other cerebral arteries, such as vertebral arteries, before entering the brain. Cold air or fluids in the nasal cavities including the epipharynx are in close thermal contact with the veins draining to the dense venous plexus surrounding the internal carotid and vertebral arteries and to the cavernous sinus. Moreover, the sub mucosal position of the carotid arteries in the epipharynx might play an additional role in this heat exchange.

The hypothesis is supported by Mariak Z et al. (J. Appl Physiol 1999; 87:1609-13) who demonstrated a slight fall of the brain temperature when intubated patients (no cold venous blood from nasal cavities) were extubated and were allowed to breathe normally and this in spite of the poor heat conduction of air.

According to the present invention, a selective hypothermia treatment of the brain in patients with brain ischemia, such as stroke and cardiac arrest, is disclosed, and a technique that can also include patients with hyperthermia. This technique can also be used for increasing the temperature of the brain.

An object of the present invention is to provide a system and a method for quick and efficient control of the

temperature of the brain without substantially changing the temperature of the rest of the body.

Another object of the invention is to provide a system and a method that is simple and initially does not require specialized personnel acquainted with for example radiology or other diagnostic imaging techniques.

In a first aspect of the invention, there is provided a system for indirect temperature regulation of substantially the brain of a human being via a nasal cavity thereof, comprising a membrane adapted to be arranged in contact with a surface of said nasal cavity, said membrane defining a closed volume; an inlet means for introducing fluid into said volume and an outlet means for removing fluid from said volume; and means for circulating said fluid into said volume via said inlet means and out of said volume via said outlet means. The system may further comprise a cooling member for introducing temperature regulated fluids into said nasal cavities, whereby said fluid can be either in direct contact with said nasal cavities or separated from said nasal cavities by said membrane.
In an embodiment, the system comprises a double lumen catheter means introduced through a nostril of a human being and placed with its tip adjacent the back of said nasal cavities, said double lumen catheter means comprising a first lumen and a second lumen, said first and second lumens being in fluid communication by means of a set of openings, said second lumen being configured as an expandable balloon; a reservoir comprising a fluid; and means for circulating said fluid from said reservoir into said double lumen catheter means and back to said reservoir or to a receptacle, whereby said balloon, when in use, is expandable

to cover the inner surface of the nasal cavity. A temperature regulator may be connected to the reservoir, said regulator being configured to regulate the temperature of said fluid, via a cooling device. The means for circulating said temperature regulated fluid may comprise a set of tubings configured to connect said catheter means to said reservoir or said receptacle.

In another embodiment, the double lumen catheter means may comprise: an inlet in fluid communication with said reservoir and with said first lumen, said inlet being configured to receive said fluid from said reservoir; said first lumen having a set of distal end openings in a front end portion of said catheter means, said end openings being arranged in fluid communication with said second lumen; and an outlet in fluid communication with said second lumen and with said reservoir or said receptacle. The inlet and outlet may be arranged at a proximal portion of the catheter means. The circulation of said fluid may be accomplished by means of hydrostatic pressure of said fluid in said reservoir. Alternatively, the means for circulating said fluid further may comprise a pumping means arranged between said reservoir and said catheter means. The means for circulating the fluid may be configured to provide a flow rate of approximately 25 - 1000 ml/min. The system may further comprise a pressure regulating nozzle arranged at said tubings adjacent said reservoir or said receptacle, said pressure regulating nozzle being configured to provide a resistance in said tubings, said pressure regulating nozzles being possibly variable.

In a further embodiment, the system may further comprise a temperature monitoring device configured to, indirectly or

directly, register the temperature of the brain and to automatically control said temperature regulator to regulate the temperature of said fluid in said reservoir, via a heat exchanging device, in order to maintain the temperature of the brain at a desired level. The temperature monitoring device may be an IR thermistor, a MR device, a Near InfraRed device or an impedance spectroscopy device. The temperature monitoring device may be arranged on the skin, such as the forehead, of the human being or in an auditory canal of the human being. The temperature of the brain may be approximately 10 - 41°C, such as 20-35°C. The catheter means may be manufactured of a material such as plastic, synthetic latex, silicone or Gore-Tex. The material may be coated with a hydrophilic surface or an anaesthetic agent.

In another aspect of the invention, there is provided a kit of disposables for use in the system mentioned above, comprising a plurality of tubings and double lumen catheter means.

In a further aspect, there is provided a method for indirect temperature regulating of substantially the brain of a human being via a nasal cavity thereof, comprising the steps of: introducing a double lumen catheter means through a nostril into said nasal cavity of said human being, said double lumen catheter means comprising a first lumen and a second lumen, said first and second lumens being in fluid communication by means of a set of openings, said second lumen being configured as an expandable balloon; placing said catheter means with its tip adjacent the back portion of said nasal cavity; temperature regulating a fluid in a reservoir; circulating said fluid from said reservoir into said double lumen catheter means back to said reservoir or

to a receptacle, whereby said balloon is expanded to cover the inner surface said nasal cavity. The step of circulating said fluid may comprise the step of pumping said fluid from said reservoir into said catheter means and back to said reservoir via said first and second lumens by means of a pumping means. The step of circulating said fluid may be accomplished by means of the hydrostatic pressure of said fluid in said reservoir. The fluid may circulate at a flow rate in the interval of approximately 25 - 1000 ml/min.

In an embodiment, the method may further comprise the step of placing a temperature sensor on the human being; directly or indirectly registering a brain temperature by means of said temperature sensor; and temperature regulating said fluid, via a heat exchanging device, in dependence of said registered brain temperature in order to maintain the brain temperature at a desired level. The step of temperature regulating said fluid may comprise the step of cooling said fluid in order to obtain a brain temperature of approximately 10 - 41°C, preferably 20-35°C.

In a still further aspect, there is provided a system for indirect temperature regulation of substantially the brain of a human being via a nasal cavity thereof, comprising: a first balloon catheter means introduced through a first nostril into said nasal cavity, said first balloon catheter comprising a first balloon and a second balloon, said first balloon being placed at the back of said nasal cavity and being configured to occlude the nasal entrance to the mouth, said second balloon being placed at the opening of said first nostril and being configured to occlude said first nostril; a second balloon catheter means introduced through a second nostril of said nasal cavity, said second

balloon catheter comprising a third balloon placed at the opening of said second nostril and being configured to occlude said second nostril; a reservoir comprising a fluid; and means for circulating said fluid from said reservoir into said first nostril, through several holes in said first balloon catheter means into said nasal cavity, whereby said fluid flushes said nasal cavity and leaves through said second nostril by means of said second balloon catheter means, or the other way around.

In a yet further aspect, there is provided a method for indirect temperature regulating of substantially the brain of a human being via a nasal cavity thereof, comprising the steps of: introducing a first balloon catheter means through a first nostril of a human being, where said first balloon catheter comprises a first balloon and a second balloon; placing said first balloon at the back of said nasal cavity and said second balloon at the opening of said first nostril; expanding said first balloon to occlude the nasal entrance to the mouth and expanding said second balloon to occlude said first nostril; introducing a second balloon catheter means through a second nostril of a human being, where said second balloon catheter comprises a third balloon; placing said third balloon at the opening of said second nostril; expanding said third balloon to occlude said second nostril; temperature regulating a fluid in a reservoir; and circulating said fluid from said reservoir through said first nostril and into said nasal cavity and back through said second nostril, or the other way around.

In still yet a further aspect, there is provided a system for indirect temperature regulation of substantially the brain of a human being via nasal and mouth cavities

thereof, comprising: a first balloon catheter means introduced through a first nostril of said nasal cavity, said first balloon catheter comprising a first balloon placed at the opening of said first nostril and being configured to occlude said first nostril; a second balloon catheter means introduced through a second nostril of said nasal cavity, said second balloon catheter comprising a second balloon placed at the opening of said second nostril and being configured to occlude said second nostril; a third balloon catheter means introduced through said mouth cavity, said third balloon catheter comprising a third balloon placed in mid oesophagus of the human being and being configured to occlude said mid oesophagus; a catheter mean placed in said mouth cavity and sealed to the lips of the mouth of the human being; a reservoir comprising a fluid; and means for circulating said fluid from said reservoir into said first and second nostril, through said first and second balloon catheter means into said nasal cavity, whereby said fluid flushes said nasal cavity and leaves through said mouth by means of said catheter means.

In another further aspect, there is provided a method for indirect temperature regulating of substantially the brain of a human being via nasal and mouth cavities thereof, comprising the steps of: introducing a first balloon catheter means through a first nostril of said nasal cavity, said first balloon catheter comprising a first balloon; placing said first balloon at the opening of said first nostril; expanding said first balloon to occlude said first nostril; introducing a second balloon catheter means through a second nostril of said nasal cavity, said second balloon catheter comprising a second balloon; placing said second

balloon at the opening of said second nostril; expanding said second balloon to occlude said second nostril; introducing a third balloon catheter means through said mouth cavity, said third balloon catheter comprising a third balloon; placing said third balloon in mid oesophagus of said human being; expanding said third balloon to occlude said mid oesophagus; introducing a catheter means into said mouth cavity; sealing said catheter means to the lips of said mouth cavity; temperature regulating a fluid in a reservoir; and circulating said fluid from said reservoir into said first and second nostrils, through said first and second balloon catheter means into said nasal cavity, flushing said fluid through said nasal cavity and through said mouth cavity by means of said catheter means.

In a yet further aspect, there is provided a system for indirect temperature regulation of substantially the brain of a human being via a nasal cavity thereof, comprising: a balloon catheter means introduced through a nostril into said nasal cavity, said balloon catheter comprising a first balloon, a second balloon and an opening means, said first balloon being placed at the back of said nasal cavity adjacent a distal end of a nasal septum in said nasal cavity and being configured to occlude said nasal cavity, said second balloon being placed at the opening of said first nostril and being configured to occlude said first nostril, said opening being placed adjacent said second balloon; a reservoir comprising a fluid; and means for circulating said fluid from said reservoir into said nostril, through said opening means into said nasal cavity, whereby said fluid flushes said nasal cavity and leaves said nostril by

means of several holes in said balloon catheter means, or the other way around.

In a still yet further aspect, there is provided a method for indirect temperature regulating of substantially the brain of a human being via a nasal cavity thereof, comprising the steps of: introducing a first balloon catheter means through a nostril into said nasal cavity, where said first balloon catheter comprises a first balloon, a second balloon and an opening means; placing said first balloon at the back of said nasal cavity adjacent a distal end of a nasal septum of said nasal cavity, said second balloon at the opening of said nostril and said opening means adjacent said second balloon; expanding said first balloon to occlude said nasal cavity and expanding said second balloon to occlude said first nostril; temperature regulating a fluid in a reservoir; and circulating said fluid from said reservoir into said first nostril, through said opening means into said nasal cavity, flushing said fluid through said nasal cavity and through said nostril by means of several holes in said first balloon catheter means, or the other way around.

By means of the present invention, the naso-pharyngeal membranes can be temperature regulated, e.g. cooled or heated, whereby the cold or heat is transmitted to the adjacent arterial and venous structures, which in turn is transmitting the cold or heat to the brain. In this way, the temperature of the brain parenchyma can be reduced or increased without needing any direct contact or intervention with the vascular system.

Brief description of the drawings

Further objects, features and advantages will become evident from the following description of several embodiments of the invention with reference to the enclosed drawings, in which:

Fig 1 is a schematic view of a first embodiment of a system according to the present invention;

Fig 2 is a schematic view of a second embodiment of a system according to the present invention;

Fig 3 is a cross-sectional view of the double catheter means arranged at the inner surface of the nose, the nasal cavity, and epipharynx of a patient;

Fig 4 is a diagram showing an example of the registered temperature variation in the brain as a function of the time, when the inventive system and method is applied to a laboratory animal in the form of a pig;

Fig 5 is a schematic view of two temperature sensors, each of which is arranged in an auditory channel;

Fig 6A is a cross-sectional view of another embodiment of a system according to the present invention;

Fig 6B is a cross-sectional view similar to Fig 6A of the other nasal cavity;

Fig 6C is a cross-sectional view similar to Fig 6A of yet another embodiment of the invention;

Fig 7 is a top view of the head including the embodiment shown in Fig 6A-6B;

Fig 8 is a diagram of different combinations of cooling techniques;

Fig 9A is a cross-sectional view of still another embodiment of the invention; and

Fig 9B is a cross-sectional view of one more embodiment of the invention.

Detailed description of the invention

The present invention will now be described with reference to the accompanying drawings.

Fig 1 discloses a first embodiment of an inventive system 10 for cerebral temperature control of a human being, in which embodiment the system comprises one double lumen catheter means 30.

Fig 2 shows schematically a second embodiment of the inventive system, which system comprises two double lumen catheters means 30a, 30b to be introduced in respective nostril of a human being. By means of two catheter means, temperature regulation may be accomplished more effectively and quicker.

In the figures, the same reference numerals are used to indicate corresponding components. Further, in Fig 2, the corresponding components and details of the respective catheter means are distinguished by means of the addition of the letter a respective b to the reference numeral. Arrows are used to show the flow direction of the fluid in the system. However, as understood by the skilled person, the fluid flow can have the opposite direction to that indicated in the drawings.

The system 10 comprises a double lumen balloon catheter means 30, 30a, 30b configured to be introduced through a nostril of a human being and to be placed with its tip at the level of the back of the nasal cavities, as shown in Fig 3. Pushing a sleeve or sheath 39 backward or forward may vary the length of double lumen balloon catheter.

The double lumen catheter means 30, 30a, 30b comprises a first lumen 32, 32a, 32b and a second lumen 38, 38a, 38b. The first and second lumens are arranged in fluid communication with each other by means of a set of end openings 34, 34a, and 34b. The second lumen 38, 28a, 38b is configured as an expandable balloon.

The system 10 could also comprise a temperature regulator 24, shown in Fig 2, connected to a reservoir 20 comprising a fluid 22. The temperature regulator 24 is configured to regulate the temperature of the fluid 22 comprised in the reservoir. The fluid 22 is for example a saline solution. The temperature regulator controls a heat exchanging device, normally a cooling device, for temperature regulating the fluid.

Means are arranged in the form of tubes 12, 12a, 12b, 14, 16, 16a, 16b for circulating said temperature regulated fluid 22 from the reservoir 20 to the catheter means 30, 30a, and 30b. The means 12, 12a, 12b, 14, 16, 16a, 16b are configured to circulate the fluid 22 into the first lumen 32, 32a, 32b of the catheter means 30, 30a, 30b, from the first lumen 32, 32a, 32b into the second lumen 38, 38a, 38b, and from the second lumen 38, 38a, 38b back to said reservoir 20, or vice versa.

The circulation means 12, 12a, 12b, 14, 16, 16a, 16b for circulating said temperature regulated fluid 22 comprises a set of tubings 12, 12a, 12b, 14, 16, 16a, 16b configured to connect the catheter means 30, 30a, 30b to the reservoir 20.

In use, when the fluid enters the second catheter 38, 38a, 38b, the second catheter 38, 38a, 38b is expanded more or less as a balloon to completely or almost completely

cover the inner surface of the nose and epipharynx, as shown in Fig 3, whereby the naso-pharyngeal membranes may be temperature regulated. The temperature is transferred to adjacent arterial and venous structures, which are transferring the temperature to the brain.

Further, by means of the inventive arrangement the temperature regulated fluid 22 circulates in a closed fluid system 12, 12a, 12b; 14; 16, 16a, 16b; 30a, 30b; 20.

The inventive double lumen catheter means 30, 30a, 30b comprises an inlet 31, 31a, 31b arranged to provide fluid communication with the reservoir 20 and with the first lumen 32, 32a, and 32b. The inlet 31, 31a, 31b is further configured to receive an amount of the temperature regulated fluid 22 from the reservoir 20. The first lumen 32, 32a, 32b has a set of distal end openings 34, 34a, 34b in a front-end portion 36, 36a, 36b of the catheter means 30, 30a, and 30b. The end openings 34, 34a, 34b being arranged to provide fluid communication with said second lumen 38, 38a, and 38b. The catheter means 30, 30a, 30b further comprises an outlet 33, 33a, 33b configured to provide fluid communication with the second lumen 38, 38a, 38b and with the reservoir 20.

The inlet 31, 31a, 31b and the outlet 33, 33a, 33b are arranged at an end portion 40, 40a, 40b of the catheter means 30, 30a, 30b.

According to an embodiment, the second lumen 38, 38a, 38b has a variable length L of approximately 5 - 25 cm. The sleeve 39 around the shaft of the catheter can reduce the length L of the second lumen when the sleeve is moved backward or forward. In expanded state, the diameter A of the second lumen at a front part 36, 36a, 36b of the second lu-

men is approximately 2 - 4 cm and the diameter B of the second lumen at a base part 37, 37a, 37b of the second lumen is approximately 1 - 3 cm, but these measures can vary if the balloon pressure is increased.

The catheter means 30, 30a, 30b could be manufactured of a flexible material such as plastic, synthetic latex, silicone or Gore-Tex. The material may be coated with a substance resulting in a hydrophilic surface. An anesthetic agent may also cover the surface.

According to an embodiment of the invention, the circulation of the fluid 22 is accomplished by means of the hydrostatic pressure of the fluid 22 in the reservoir 20. As shown in Fig 1, the reservoir 20 is arranged at a level, which is higher than the nasal cavity of the human being under treatment, and a waste bag 29 is arranged below the same level. Thence, the cold fluid flows by gravity from the reservoir and to the catheter device and further to the waste bag.

However, according to another embodiment of the invention, the means 12, 14, 16 for circulating the temperature regulated fluid 22 further comprises a pumping means 18 arranged between the reservoir 20 and the catheter means 30, 30a, 30b by means of tubings 12, 12a, 12b, 14. Thus, it should be understood that the pumping means 18 illustrated in Fig 2 is optional.

The circulation means for circulating the fluid is preferably configured to provided a fluid flow rate of 25 - 1000 ml/min.

The inventive system can also comprise a pressure regulating nozzle 26, 26a, 26b, shown in Figs 1 and 2, arranged at the tubings 16, 16a, and 16b. The pressure regu-

lating nozzle 26, 26a, 26b is arranged close to the reservoir 20 or the waste bag 29 and being configured to provide a resistance in the tubings, whereby the fluid flowing in the system is able to expand the second lumen 38, 38a, 38b. The nozzle may be a clamp that is adjustable.

Moreover, pressure sensors 49 may be arranged for measuring the pressure in the second lumen, as shown in Fig 1. Such a pressure sensor may be a similar construction as the second lumen arranged in a side branch. By means of the pressure sensor, it can be assured that the pressure will not be too high, which may be experienced to be uncomfortable. The pressure sensor may as well be conventional pressure meters.

The technique according to the present invention involves the following, as shown in Fig 3. Two double lumen thin walled balloon catheters are inserted into the nostrils of the patient. When inflated and circulated with fluid, e.g. saline, at a temperature of ±0 to 41°C, preferably 20-35°C, at a rate of 25 to 1000 ml per min, the lower range for neonate, the balloons will cover the inner surfaces of the nose and the epipharynx, collectively named the nasal cavities. Circulation can be performed in either direction. Cooling of the nasal cavities can then be accomplished without any fluids entering the trachea or the esophagus. Different sizes of catheters and balloons will fit neonates to adults and a sheath or sleeve around the shaft of the catheter can reduce the length of the balloon when the sheath is moved forward.

In an alternative embodiment shown in Fig 6A and 6B, a double balloon catheter 60, shown in Fig 6A, which has a balloon 62 at its distal end and is introduced into a nos-

tril and advanced into the epipharynx. This balloon is provided with two small catheters (not shown), one for infusion of cold fluids and the other for extraction of these fluids into the balloon. When this balloon is inflated and retracted it lifts the soft palate, which then obliterates the passage between the nostrils and the epipharynx. At the same time this balloon acts in cooling the tissues at this level of epipharynx where especially the carotid artery lies very superficial. Another, more proximal balloon 64 on this catheter obliterates the entrance to the same nostril when inflated. A single balloon catheter 68 is introduced into the other nostril, shown in Fig 6B, the balloon when inflated obliterates the nostril and the catheter ends immediately distal to the balloon.

Multiple side holes on the double balloon catheter 60 between the balloons permit infusion of cold saline (0 - 25°C) for example at a rate of 25 - 1000 ml/ min into the nostrils. The fluid is evacuated through the other nostril catheter 68. The lumen of this catheter 68 has no connection to the more distal balloon 70.

The system can also comprise a temperature sensor 50, which is connectable to the temperature regulator 24 and configured to register or estimate the temperature of the brain and to automatically control the temperature regulator 24 to regulate the temperature of the fluid in the reservoir 20 in order to maintain the temperature of the brain at a desired level. The temperature sensor is for example an IR thermistor, which could be arranged in an auditory canal of the human being or on the skin, such as the forehead, of the human being. The temperature could also be monitored by a MR device, a Near Infrared device or an im-

pedance spectroscopy device. The desired brain temperature level may be approximately 10 - 35°C. The temperature level depends on the degree of hypothermia, which is clinically relevant. If the brain temperature is increased it should be closely monitored.

The present invention also relates to a kit of disposables for use in the inventive system. The kit comprises a plurality of tubings, and the double lumen catheter means 30, 30a, 30b.

The invention relates also to a method for cerebral temperature control. The method comprises the steps of:

introducing the double lumen catheter means 30, 30a, 30b through the nostril of the human being;

placing the catheter means 30, 30a, 30b with its tip at the level of the back of the nasal cavities;

temperature regulating the fluid 22 in the reservoir 20;

circulating the fluid from the reservoir into a first lumen 32, 32a, 32b of the catheter means, from the first lumen into a second lumen 38, 38a, 38b of said catheter means, and from said second lumen back to said reservoir, whereby the second lumen is expanded like a balloon to completely cover the inner surface of the nasal cavities and epipharynx and whereby said temperature regulated fluid circulates in a closed fluid system.

The step of circulating said temperature regulated fluid could also comprise a step of pumping said fluid from said reservoir, to said catheter means and back to said reservoir via said first and second lumens by means of a pumping means.

The temperature-regulated fluid circulates at a flow rate in the interval of approximately 25 - 1000 ml/min, depending of the size of the human being. The flow could be at the lower range for neonates.

The method can further comprise the steps of using a temperature sensor for registering the brain temperature and regulating the fluid in dependence of said registered brain temperature in order to maintain the brain temperature at a desired level.

The step of temperature regulating said fluid comprises the step of cooling said fluid in order to obtain a brain temperature of approximately 10 - 35°C.

Fig 4 schematically shows how the registered temperature in the left and right brain hemisphere is reduced after the onset of the inventive method, while the registered temperature in the rectum remains almost unchanged. In the performed experiment, a double lumen catheter means was introduced in respective nostril of an experimental animal. The temperature regulator controls the fluid temperature to desired level through a cooling element. Circulation of cold fluid started approximately at 10:18 and stopped approximately at 10:41 (after 23 minutes). As seen from Fig 4 the registered temperature in the left and right brain hemisphere is reduced within a short period of time after the start and increases again after the stop. Further, the temperature of the rectum is almost unchanged. Thus, a selectively cooling of the brain is accomplished.

As an example, another embodiment of the invention will now be described with reference to Figs 6A and 6B. A double balloon catheter 60, shown in Fig 6A, is introduced through one nostril. The inner or distal balloon 62, when

expanded, fixates the soft palatinum and occludes the entrance to the mouth. The distal balloon is supplied with fluid by two small diameter catheters, one for infusion of cold saline, and the other for extraction of the same fluid. A pressure regulating nozzle keeps the balloon expanded. The cold saline cools the area around the expanded distal balloon.

The second or proximal balloon 64 is configured to occlude the nostril.

A second balloon catheter 68 (see Fig 6B) is placed into the other nostril, the second balloon catheter 68 having a proximal balloon 70 configured to occlude the nostril.

A temperature regulated fluid, e.g. cold saline, is injected into the first catheter 60 and leaves through side holes 66 arranged lengthways the first catheter 60. The cold saline flushes the cavum nasae and epipharynx and passes beyond the wall between the two nasal cavities and leaves through the contra lateral nostril, whereby the naso-pharyngeal membranes are temperature regulated.

Other alternative designs may include that the distal balloon 62 is arranged in the nasal cavity closer to the nostril, somewhere in front of the end of the nasal septum, delimiting only a portion of the nasal cavity, as shown in Fig 6C. The cooling fluid may enter the delimited portion of the nasal cavity via the catheter 60 and holes 66 therein and leave via a separate outlet catheter 69 adjacent the proximal balloon 64 (not shown in the drawings).

The introduction of these balloon catheters into the nostrils of the patient will make rapid selective brain cooling possible. At the arrival into the hospital admis-

sion, suitable alternatives (see Fig 8) for the continuation of the hypothermia treatment are decided according to the condition of the patient.

Paramedic's start at the site an intravenous infusion of ice cooled lactated Ringers solution, possibly combined with naso-pharyngeal cooling or the treatment starts with naso-pharyngeal cooling alone.

Depending on the condition of the patient at the arrival to the hospital the following alternatives for future treatment can be seen in the admission flow chart according to Fig 8.

Patients with naso-pharyngeal cooling or retro perfusion treatment at the admission unit are later referred to the ward for future treatment according to Fig 8.

Another embodiment is used for patients with tracheostomy or tracheal intubation, shown in Fig 9A and 9B, respectively, where an esophageal balloon catheter 80 is introduced through the mouth and the balloon 81 is inflated in mid esophagus. Further balloon catheters 68', 68'', same as described in connection with Fig 6B, are placed into each nostril and the balloons 70', 70'' are inflated to occlude the nostrils. A large diameter catheter 82, not shown, is placed in the mouth and sealed to the lips for example with the aid of tapes. Cold, 5-25°C, Ringer lactate fluid or saline solution is infused through the catheters 68' into the nasal cavities at the rate of 100-1000 ml/min and evacuated through the catheter 82 in the mouth to a container. Flushing the muscosal cavities of the nose, epipharynx, pharynx and mouth with cold solution will act in the same way as described above.

It should be understood that the pumping means, tubings, fluid reservoir, temperature regulated means or other elements described above can be used in the last-mentioned embodiments.

According to the invention, the tissue in the nose and epipharynx are cooled, either with direct contact with a cooling fluid (Fig 6A) or via a membrane in contact with the tissue. In the present specification and claims, the expression "nasal cavity" is used to mean all inside surface of the nose (via both nostrils) and including the epipharynx. In some embodiments, only a portion of the nasal cavity surfaces is used for cooling purpose, and this is intended to be within the scope of the invention.

The cooling effect of the fluid can be monitored by measuring the inlet and outlet temperature of the fluid as well as the flow rate, as indicated in Fig 6C with temperature measuring unit ΔT connected to a thermocouple arranged in the inlet and outlet openings. By calorimetric calculations, the cooling effect can be calculated. If it is presumed that the heat generation of the brain or tissue inside the head is relatively constant, the temperature decrease can be calculated or predicted. Furthermore, temperature measurements at different places of the body and with different methods as indicated above, can provide further data for a closer prediction of the brain temperature.

The intention of the invention is to cool substantially only the brain, including adjacent tissue, but maintain the temperature of the rest of the body at normal temperature. It may be that the body temperature may also be lowered and this tendency may be counteracted by covering

part of the body by a blanket or by providing slightly heated warm air.

The present invention has been described with reference to embodiments and an example. However, it should be understood that modifications of components or functional steps could be performed without deviating from the scope of the invention.

CLAIMS

1. A system for indirect temperature regulation of substantially the brain of a human being via a nasal cavity thereof, comprising

a membrane adapted to be arranged in contact with a surface of said nasal cavity, said membrane defining a closed volume;

an inlet means for introducing fluid into said volume and an outlet means for removing fluid from said volume; and

means for circulating said fluid into said volume via said inlet means and out of said volume via said outlet means.

2. The system of claim 1, further comprising

a cooling member for introducing temperated fluids into said nasal cavities, whereby said fluid can be either in direct contact with said nasal cavities or separated from said nasal cavities by said membrane.

3. The system of claim 1 or 2, further comprising:

a double lumen catheter means (30) introduced through a nostril of a human being and placed with its tip adjacent the back of said nasal cavities, said double lumen catheter means comprising a first lumen (32) and a second lumen (38), said first and second lumens being in fluid communication by means of a set of openings (34), said second lumen being configured as an expandable balloon;

a reservoir (20) comprising a fluid (22);

means for circulating said fluid from said reservoir into said double lumen catheter means and back to said reservoir or to a receptacle (29),

whereby said balloon, when in use, is expandable to cover the inner surface of the nasal cavity.

4. The system according to claim 3, wherein a temperature regulator (24) is connected to said reservoir, said regulator being configured to regulate the temperature of said fluid, via a heat exchanging device, such as a cooling device.

5. The system of claim 4, wherein said means for circulating said temperature regulated fluid comprises a set of tubings configured to connect said catheter means to said reservoir or said receptacle.

6. The system of any of the previous claims, wherein said double lumen catheter means comprises:

an inlet (31, 31a, 31b) in fluid communication with said reservoir and with said first lumen, said inlet being configured to receive said fluid from said reservoir;

said first lumen having a set of distal end openings (34, 34a, 34b) in a front end portion (36) of said catheter means, said end openings being arranged in fluid communication with said second lumen; and

an outlet (33, 33a, 33b) in fluid communication with said second lumen and with said reservoir or said receptacle.

7. The system of claim 6, wherein said inlet and outlet are arranged at a proximal portion (40, 40a, 40b) of the catheter means.

8. The system of any of the previous claims, wherein said circulation of said fluid is accomplished by means of hydrostatic pressure of said fluid in said reservoir.

9. The system of any of the previous claims, wherein said means for circulating said fluid further comprises a

pumping means (18) arranged between said reservoir and said catheter means.

10. The system of any of the previous claims, wherein said means for circulating the fluid is configured to provide a flow rate of approximately 25 - 1000 ml/min.

11. The system of of any of the previous claims, further comprising a pressure regulating nozzle (26, 26a, 26b) arranged at said tubings adjacent said reservoir or said receptacle, said pressure regulating nozzle being configured to provide a resistance in said tubings, said pressure regulating nozzles being possibly variable.

12. The system of claim 3, further comprising a temperature monitoring device (50) configured to, indirectly or directly, register the temperature of the brain and to automatically control said temperature regulator to regulate the temperature of said fluid in said reservoir, via a heat exchanging device, in order to maintain the temperature of the brain at a desired level.

13. The system of claim 12, wherein said temperature monitoring device is an IR termistor, a MR device, a Near InfraRed device or an impedance spectroscopy device.

14. The system of claim 13, wherein said temperature monitoring device is arranged on the skin, such as the forehead, of the human being or in an auditory canal of the human being.

15. The system of claim 12, wherein said temperature of the brain is approximately 10 - 41°C, such as 20-35°C.

16. The system of claim 3, wherein said catheter means is manufactured of a material such as plastic, synthetic latex, silicone or Gore-Tex.

17. The system of claim 16, wherein said material is coated with a hydrophilic surface or an anesthetic agent.

18. A kit of disposables for use in the system according to any one of the previous claims, comprising a plurality of tubings and double lumen catheter means.

19. A method for indirect temperature regulating of substantially the brain of a human being via a nasal cavity thereof, comprising the steps of:

introducing a double lumen catheter means through a nostril into said nasal cavity of said human being, said double lumen catheter means comprising a first lumen and a second lumen, said first and second lumens being in fluid communication by means of a set of openings, said second lumen being configured as an expandable balloon;

placing said catheter means with its tip adjacent the back portion of said nasal cavity;

temperature regulating a fluid in a reservoir;

circulating said fluid from said reservoir into said double lumen catheter means back to said reservoir or to a receptacle, whereby said balloon is expanded to cover the inner surface said nasal cavity.

20. A method according to claim 19, wherein said step of circulating said fluid comprises the step of pumping said fluid from said reservoir into said catheter means and back to said reservoir via said first and second lumens by means of a pumping means.

21. The method according to claim 19, wherein said step of circulating said fluid is accomplished by means of the hydrostatic pressure of said fluid in said reservoir.

22. The method according to claim 19, wherein said fluid circulates at a flow rate in the interval of approximately 25 - 1000 ml/min.

23. The method according to claim 19, further comprising the step of arranging a temperature monitoring device at the human being;

directly or indirectly registering a brain temperature by means of said temperature sensor; and

temperature regulating said fluid, via a heat exchanging device, in dependence of said registered brain temperature in order to maintain the brain temperature at a desired level.

24. The method according to claim 23, wherein the step of temperature regulating said fluid comprises the step of cooling said fluid in order to obtain a brain temperature of approximately 10 - 41°C, preferably 20-35°C.

25. A system for indirect temperature regulation of substantially the brain of a human being via a nasal cavity thereof, comprising:

a first balloon catheter means (60) introduced through a first nostril into said nasal cavity, said first balloon catheter comprising a first balloon (62) and a second balloon (64), said first balloon (62) being placed at the back of said nasal cavity and being configured to occlude the nasal entrance to the mouth, said second balloon being placed at the opening of said first nostril and being configured to occlude said first nostril;

a second balloon catheter means (68) introduced through a second nostril of said nasal cavity, said second balloon catheter comprising a third balloon (70) placed at the opening of said second nostril and being configured to occlude said second nostril;

a reservoir (20) comprising a fluid (22); and

means for circulating said fluid from said reservoir into said first nostril, through several holes (66) in said first balloon catheter means (60) into said nasal cavity, whereby said fluid flushes said nasal cavity and leaves through said second nostril by means of said second balloon catheter means, or the other way around.

26. A method for indirect temperature regulating of substantially the brain of a human being via a nasal cavity thereof, comprising the steps of:

introducing a first balloon catheter means (60) through a first nostril of a human being, where said first balloon catheter comprises a first balloon (62) and a second balloon (64);

placing said first balloon (62) at the back of said nasal cavity and said second balloon at the opening of said first nostril;

expanding said first balloon to occlude the nasal entrance to the mouth and expanding said second balloon to occlude said first nostril;

introducing a second balloon catheter means (68) through a second nostril of a human being, where said second balloon catheter comprises a third balloon (70);

placing said third balloon at the opening of said second nostril;

expanding said third balloon to occlude said second nostril;

temperature regulating a fluid (22) in a reservoir (20); and

circulating said fluid from said reservoir through said first nostril and into said nasal cavity and back through said second nostril, or the other way around.

27. A system for indirect temperature regulation of substantially the brain of a human being via nasal and mouth cavities thereof, comprising:

a first balloon catheter means (68') introduced through a first nostril of said nasal cavity, said first balloon catheter comprising a first balloon (70') placed at the opening of said first nostril and being configured to occlude said first nostril;

a second balloon catheter means (68'') introduced through a second nostril of said nasal cavity, said second balloon catheter comprising a second balloon (70'') placed at the opening of said second nostril and being configured to occlude said second nostril;

a third balloon catheter means (80) introduced through said mouth cavity, said third balloon catheter comprising a third balloon (81) placed in mid esophagus of the human being and being configured to occlude said mid esophagus;

a catheter mean (82) placed in said mouth cavity and sealed to the lips of the mouth of the human being;

a reservoir (20) comprising a fluid (22); and

means for circulating said fluid from said reservoir into said first and second nostril, through said first and second balloon catheter means (68', 68'') into said nasal cavity, whereby said fluid flushes said nasal cavity and leaves through said mouth by means of said catheter means (82).

28. A method for indirect temperature regulating of substantially the brain of a human being via nasal and mouth cavities thereof, comprising the steps of:

introducing a first balloon catheter means (68') through a first nostril of said nasal cavity, said first balloon catheter comprising a first balloon (70');

placing said first balloon at the opening of said first nostril;

expanding said first balloon to occlude said first nostril;

introducing a second balloon catheter means (68'') through a second nostril of said nasal cavity, said second balloon catheter comprising a second balloon (70'');

placing said second balloon at the opening of said second nostril;

expanding said second balloon to occlude said second nostril;

introducing a third balloon catheter means (80) through said mouth cavity, said third balloon catheter comprising a third balloon (81);

placing said third balloon in mid esophagus of said human being;

expanding said third balloon to occlude said mid esophagus;

introducing a catheter means (82) into said mouth cavity;

sealing said catheter means to the lips of said mouth cavity;

temperature regulating a fluid (22) in a reservoir (20); and

circulating said fluid from said reservoir into said first and second nostrils, through said first and second balloon catheter means (68', 68'') into said nasal cavity, flushing said fluid through said nasal cavity and through said mouth cavity by means of said catheter means (82).

29. A system for indirect temperature regulation of substantially the brain of a human being via a nasal cavity thereof, comprising:

a balloon catheter means (60) introduced through a nostril into said nasal cavity, said balloon catheter comprising a first balloon (62), a second balloon (64) and an opening means, said first balloon (62) being placed at the back of said nasal cavity adjacent a distal end of a nasal septum in said nasal cavity and being configured to occlude said nasal cavity, said second balloon being placed at the opening of said first nostril and being configured to occlude said first nostril, said opening being placed adjacent said second balloon;

a reservoir (20) comprising a fluid (22); and

means for circulating said fluid from said reservoir into said nostril, through said opening means into said nasal cavity, whereby said fluid flushes said nasal cavity and leaves said nostril by means of several holes (66) in said balloon catheter means, or the other way around.

30. A method for indirect temperature regulating of substantially the brain of a human being via a nasal cavity thereof, comprising the steps of:

introducing a first balloon catheter means (60) through a nostril into said nasal cavity, where said first balloon catheter comprises a first balloon (62), a second balloon (64) and an opening means (69);

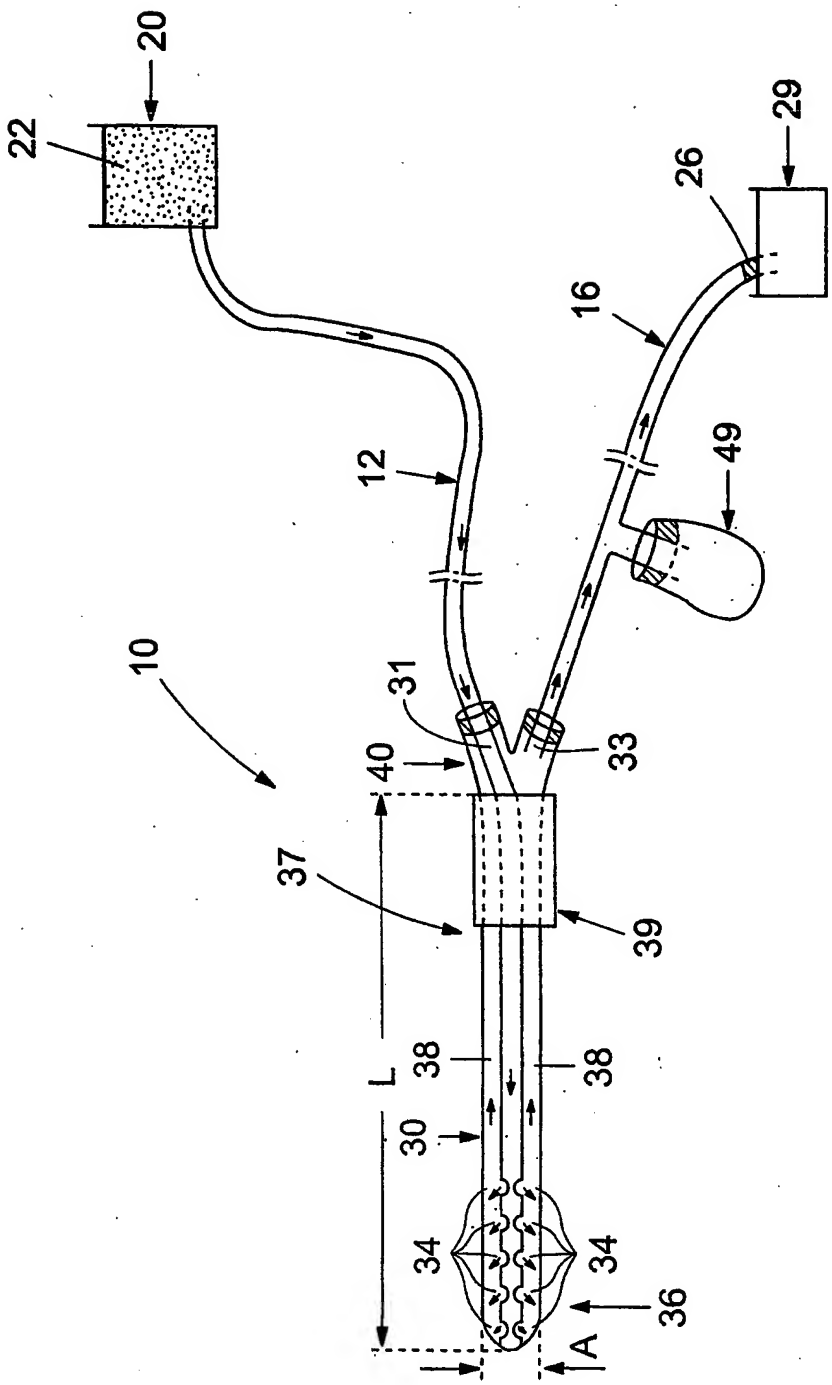
placing said first balloon (62) at the back of said nasal cavity adjacent a distal end of a nasal septum of said nasal cavity, said second balloon at the opening of said nostril and said opening means adjacent said second balloon;

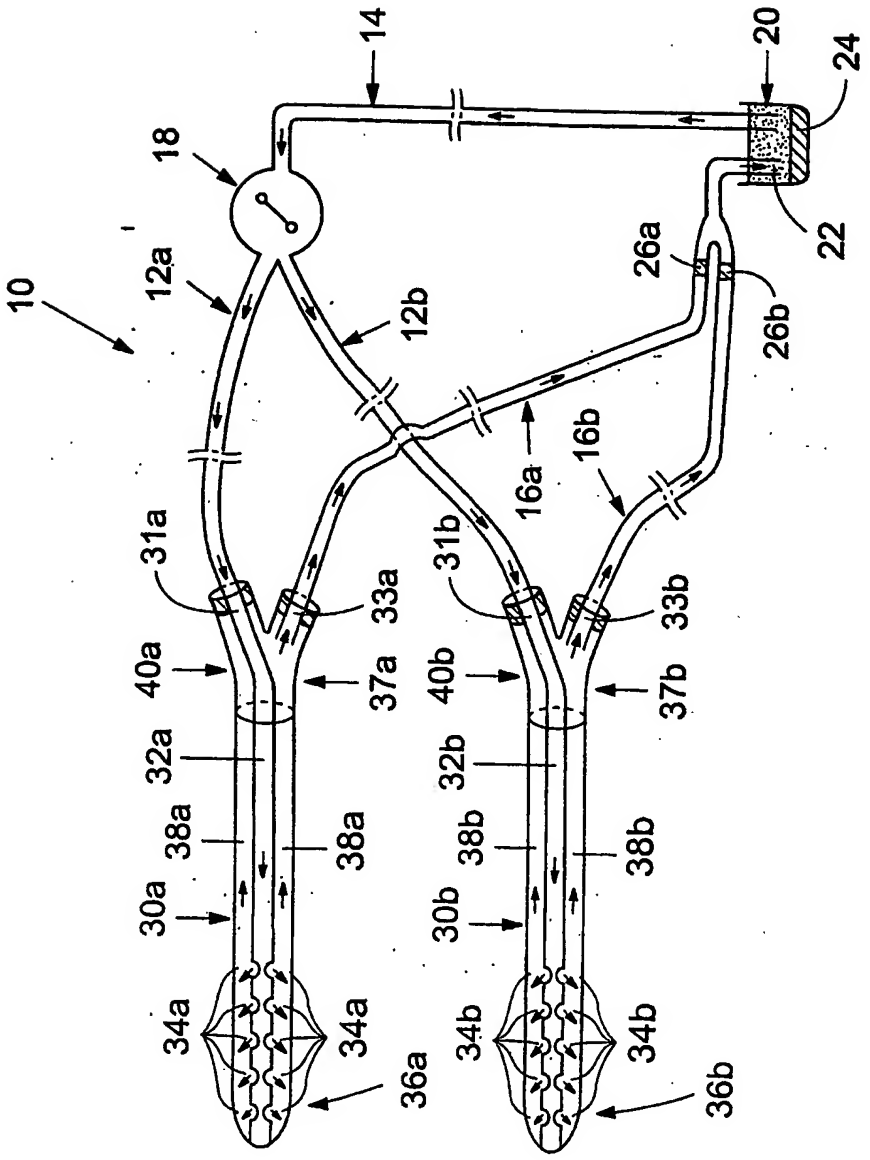
expanding said first balloon to occlude said nasal cavity and expanding said second balloon to occlude said first nostril;

temperature regulating a fluid (22) in a reservoir (20); and

circulating said fluid from said reservoir into said first nostril, through said opening means into said nasal cavity, flushing said fluid through said nasal cavity and through said nostril by means of several holes (66) in said first balloon catheter means, or the other way around.

Fig. 1

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24
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31b
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36b
37a
37b
38a
38b
40a
40b

Fig.2

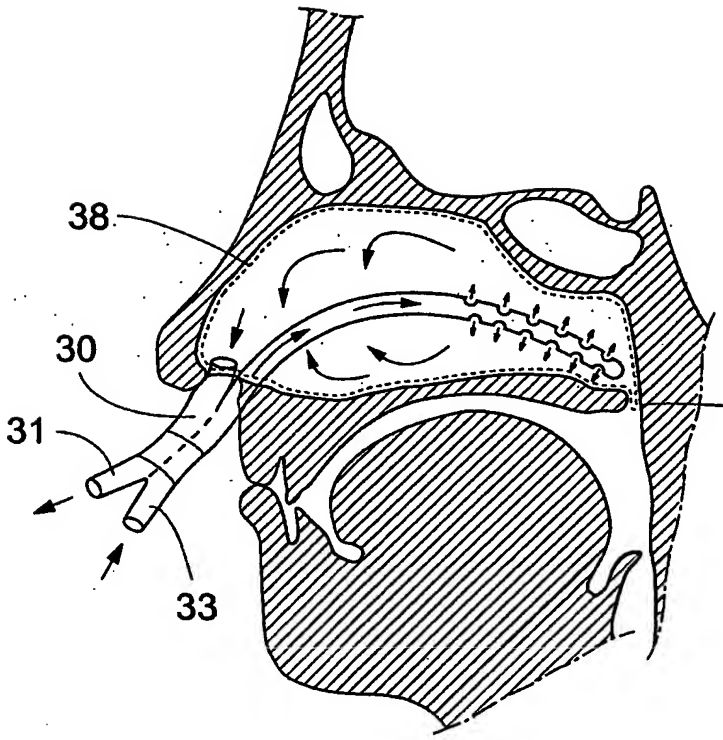
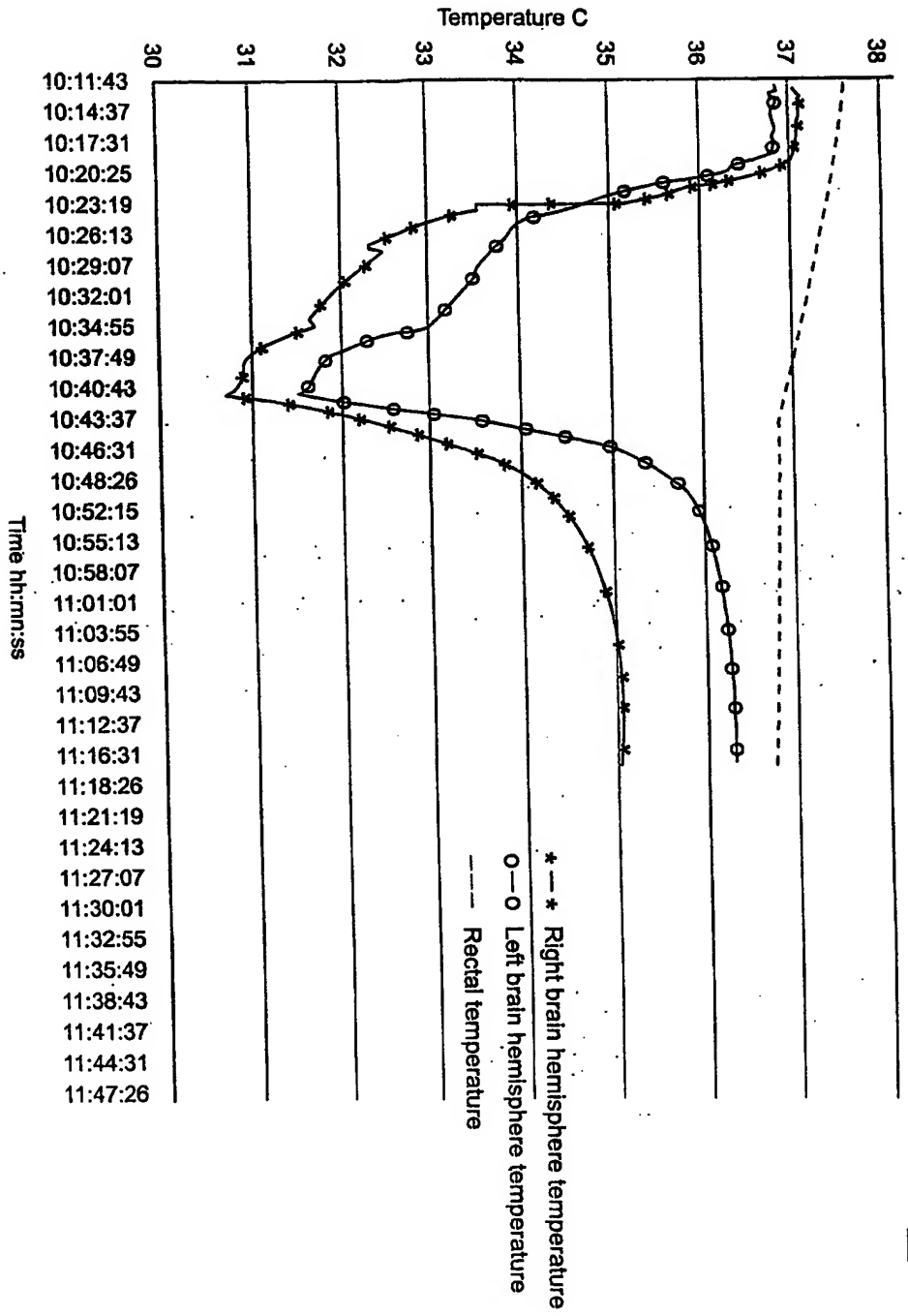


Fig.3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31
32
33
34
35
36
37
38
Time hh:mn:ss
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10:48:26
10:52:15
10:55:13
10:58:07
11:01:01
11:03:55
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11:18:26
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11:24:13
11:27:07
11:30:01
11:32:55
11:35:49
11:38:43
11:41:37
11:44:31
11:47:26
— Right brain hemisphere temperature
O—O Left brain hemisphere temperature
– – – Rectal temperature

Fig.4

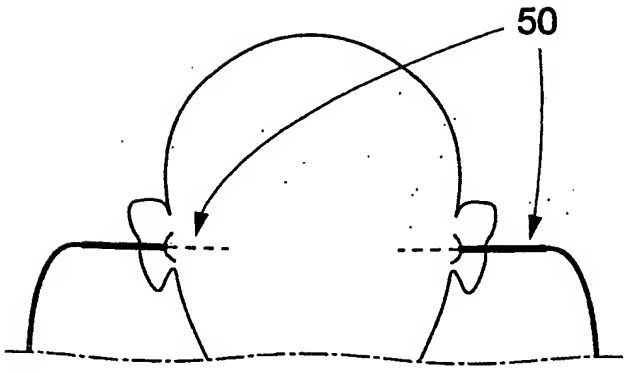


Fig.5

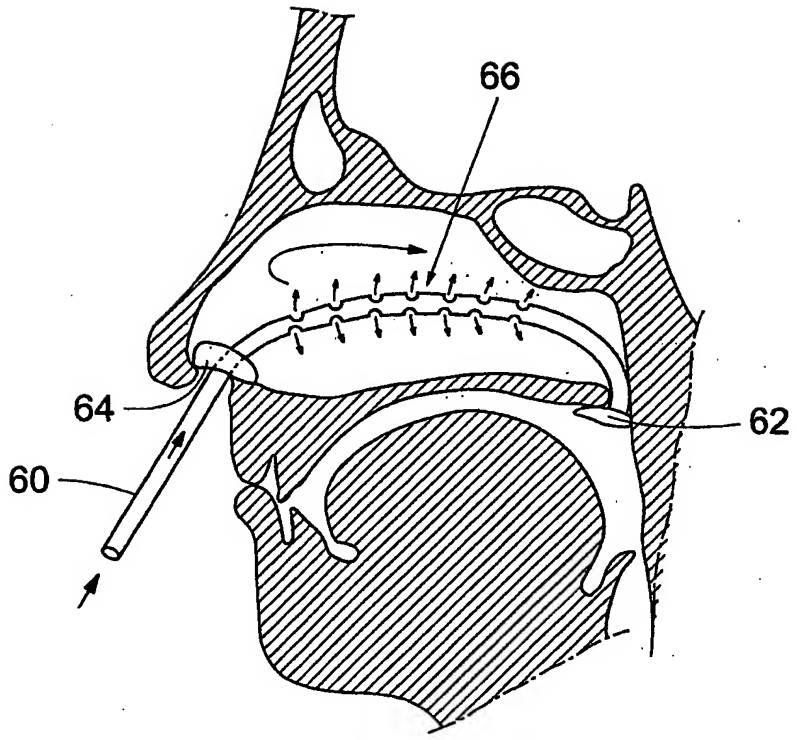


Fig.6A

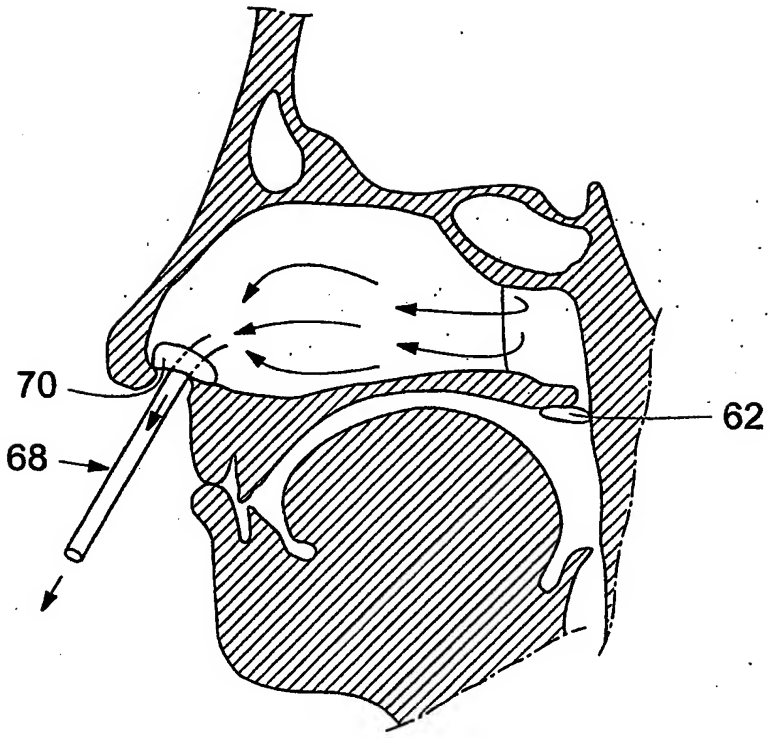


Fig.6B

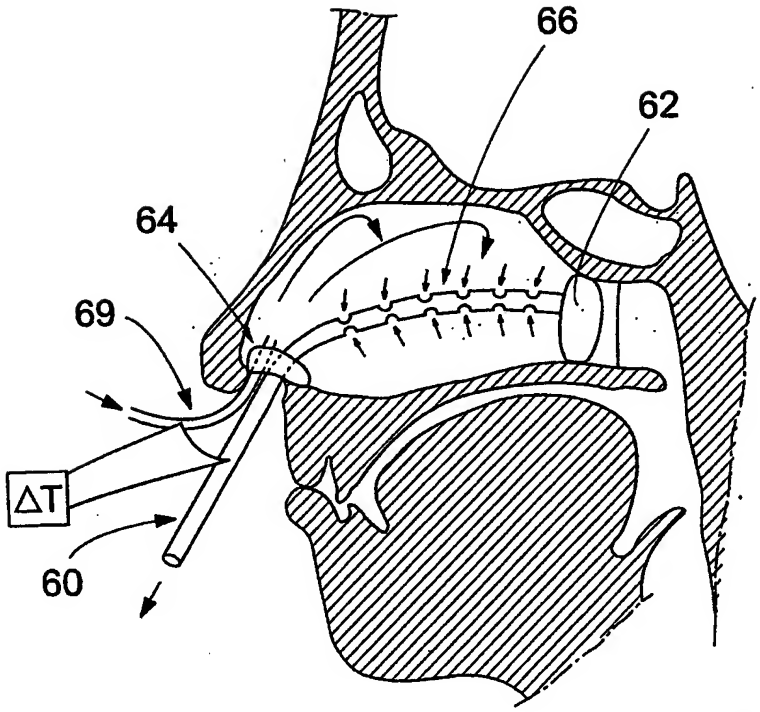


Fig.6C

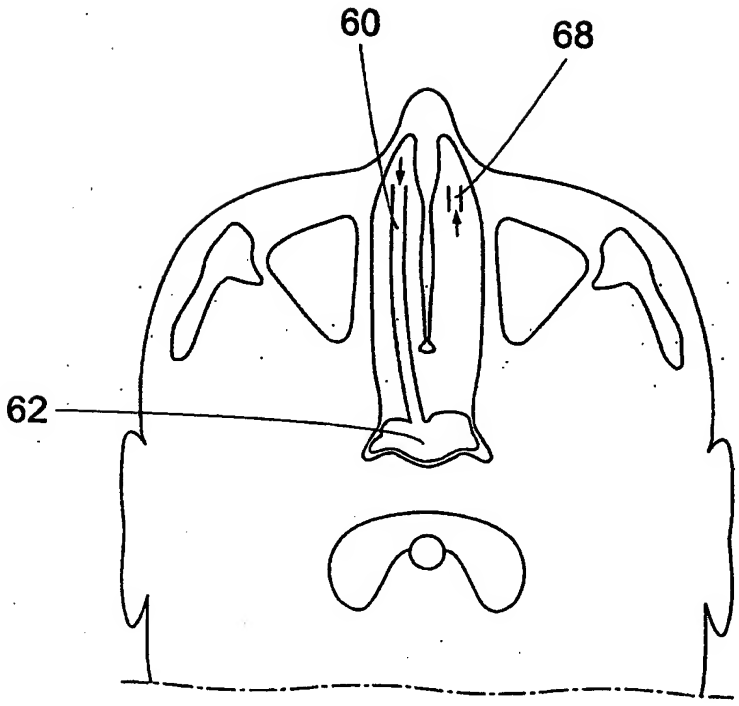
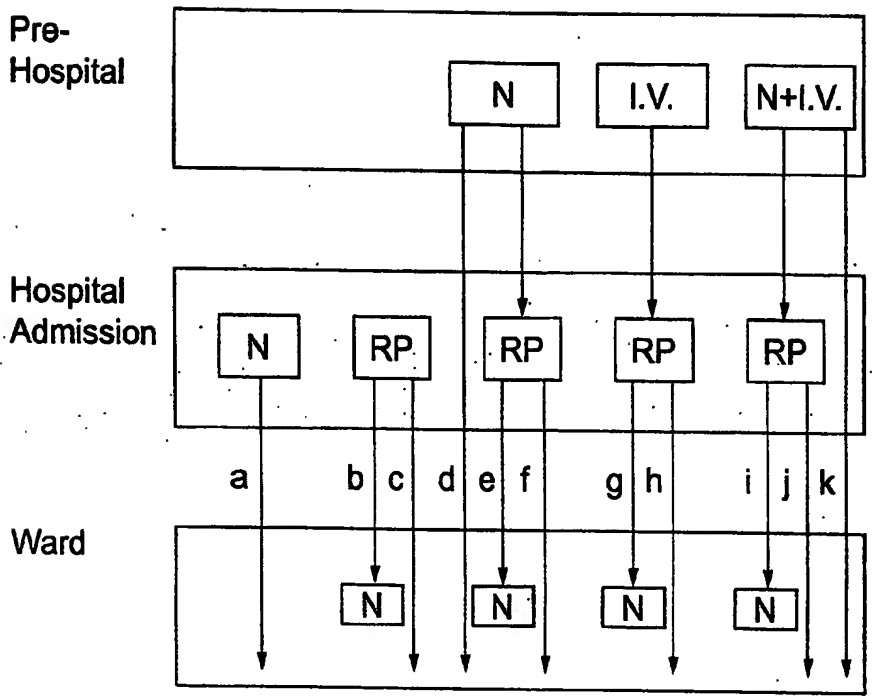


Fig.7



N: Naso-pharyngeal cooling
I.V: Intra venous infusion of cooled solution
RP: Retroperfusion cooling

Fig.8

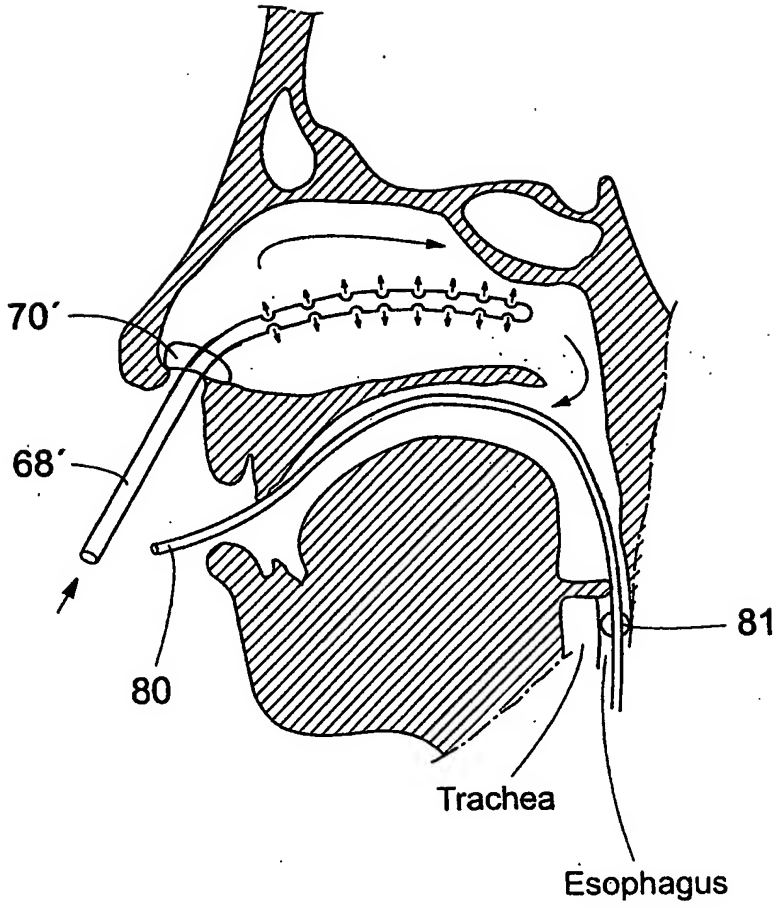


Fig.9A

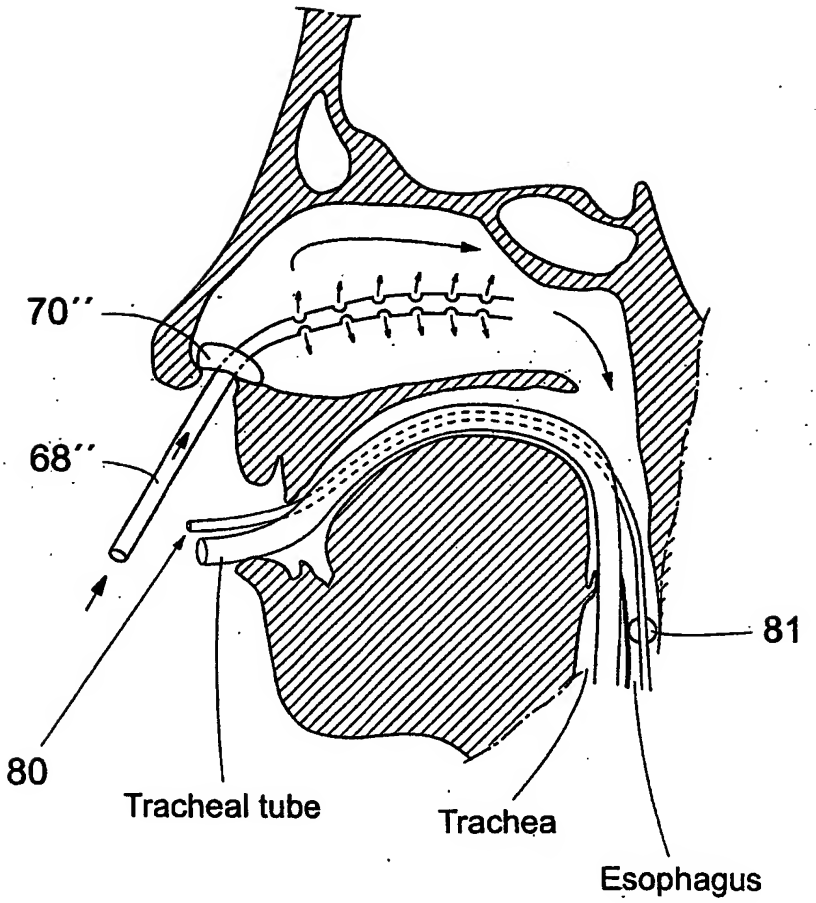


Fig.9B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2005/000382

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61F 7/12
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, WPI DATA, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 19952440 A1 (LIEKE, MICHAEL), 3 May 2001 (03.05.2001), column 3, line 21 - line 59; column 5, line 48 - column 6, line 13, abstract --	1-18,25,27, 29
X	US 5792100 A (SHANTHA), 11 August 1998 (11.08.1998), claims 1-3 --	1
X	US 20040049154 A1 (LARNARD), 11 March 2004 (11.03.2004), page 6, paragraph [0083], abstract --	1
X	US 20020138121 A1 (FOX), 26 Sept 2002 (26.09.2002), page 8, paragraph [0083], abstract --	1

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 May 2005	02 -06- 2005
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer William Helin/EK Telephone No. +46 8 782 25 00

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2005/000382

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3766924 A (PIDGEON), 23 October 1973 (23.10.1973), figure 2, abstract ---	1-8,25,27,29
A	US 20020161349 A1 (ALLERS ET AL), 31 October 2002 (31.10.2002), cited in the application --	1-18,25,27, 29
A	WO 9823217 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA), 4 June 1998 (04.06.1998), cited in the application -- --------	1-18,25,27, 29

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2005/000382

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 19-24,26,28,30
because they relate to subject matter not required to be searched by this Authority, namely:

a method of treatment of the human or animal body by surgery or by therapy /Rule 39.1(iv).

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

DE	19952440	A1	03/05/2001	NONE			
US	5792100	A	11/08/1998	US	5735817	A	07/04/1998
US	20040049154	A1	11/03/2004	US	6743200	B	01/06/2004
				US	20020091428	A	11/07/2002
				US	20040167468	A	26/08/2004
				CA	2425015	A	11/04/2002
				CA	2425059	A	11/04/2002
				CA	2425061	A	11/04/2002
				CA	2425106	A	11/04/2002
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				EP	1326562	A	16/07/2003
				EP	1326563	A	16/07/2003
				EP	1326564	A	16/07/2003
				US	6648907	B	18/11/2003
				US	6652566	B	25/11/2003
				US	6660026	B	09/12/2003
				US	20020068902	A	06/06/2002
				US	20020091425	A	11/07/2002
				US	20020116040	A	22/08/2002
				US	20020123783	A	05/09/2002
				US	20040034321	A	19/02/2004
				US	20040049250	A	11/03/2004
				WO	0228328	A	11/04/2002
				WO	0228329	A	11/04/2002
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